ACEI Relation with Cardiac Enzyme CK-MB Levels in Hypertensive Patients

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Abstract

Captopril is one of ACEI (Angioten Converting Enzyme Inhibitor). It is widely used for treatment of hypertension as effective and safe antihypertensive drug. But long term usage of Captopril may cause one of the cardiovascular diseases like myocardial infarction. To prove the relationship between Captopril and cardiovascular disease, measurement of creatine-kinase-MB as a diagnostic indicator in early and long term usage of this drug by hypertensive patients is recommended.

A comparative study was conducted in Al-Yarmouk Teaching Hospital-Emergency Department- on 24 hypertensive patients using Captopril. They were divided into (2) groups A and B according to the duration of the drug usage. Group A (12) patients with a mean age (51) years.

They used Captopril for a period of (1-5) years. Group B also (12) patients with mean age (56) years. They used Captopril for (6-12) years. Both groups were with nearly the same number of males and females. Venous blood samples were taken in first 8 hours after onset symptoms of cardiac attack from each patient and the levels of creatine kinase-MB were estimated and compared between the two groups. There is significant correlation between levels of serum creatine kinase-MB of group A and group B ($p<0.05$). Captopril causes increased level of serum CK-MB and this increase was directly proportional to the duration of the drug usage CK-MB the specific marker for cardiovascular diseases. So, Captopril has a significant correlation with development of cardiovascular diseases.

A comparative study with another antihypertensive drug Atenolol taken by a group of (24) patients using Atenolol for 1-12 years, showed a significant correlation between levels of serum CK-MB of the two groups of patients using Atenolol for a period of (1-5) years and (5-12) years ($p<0.05$). Non-significant correlation between levels of serum CK-MB of the two groups of patients that use Captopril and Atenolol for (1-5) years ($p=0.085$). A significant correlation between levels of serum CK-MB of the two groups of patients that use Captopril and Atenolol for (6-12) years ($p<0.05$). Captopril showed less effect on levels of CK-MB than Atenolol did.

Key words: hypertension, Captopril, ACEI, creatine kinase-MB, Captopril antihypertensive, Atenolol antihypertensive.

Introduction:

Captopril is one of Angiotensin Converting Enzyme (ACE) inhibitor, used in the treatment of hypertension and heart failure[1], myocardial infarction[2] and diabetic nephropathy [3]. Captopril leads to decreased production of Angiotensin II and aldosterone which are important in constricting the blood vessels, and conserving salt and water, both of which increase blood pressure [4]. Inhibition of ACE results in decreased plasma Angiotensin II and increased plasma rennin activity, and reduction of Angiotensin II leads to decreased aldosterone secretion, and as a result increases in serum potassium may occur along with sodium and fluid loss [5]. After oral administration of therapeutic doses of capeton, rapid absorption occurs with peak blood levels at about one hour. In a 24-hour period, over 95 percent of the absorbed dose is unchanged drug. Captopril results in a reduction of peripheral arterial resistance in hypertensive patients, with either no change, or an increase in cardiac output. In addition there is an increase in renal blood flow and glomerular filtration rate is usually unchanged [5].

Common side effects of Captopril are low blood pressure, cough [6], rash and taste disturbances [1], in addition there may be other serious side effect associated with cardiac disease with long term usage of Captopril [7].

Creatine kinase-MB is one of the isoenzyme of creatine kinase which is mostly found in the heart. In this study, the CK-MB was measured as an important biological marker. When it appears in abnormal level >10u/L in serum, this means that there is a myocardial injury [8]. CK-MB shows an increase above normal in a person's blood test about four to six hours after the start of heart attack, it reaches its peak level in about 18 hours and returns to normal in 24 to 36 hours [9]

CK-MB is a sensitive and specific marker for myocardial infarction [10], and it is most commonly used to confirm the existence of heart muscle damage [11, 12].

Materials & Methods:

This research is a comparative study in the Emergency Department in Al-Yarmouk Teaching Hospital. Twenty four hypertensive patients (45-69) years who received Captopril tablet as antihypertensive drug for duration of (1-12) years were included in the study. The patients were divided into (2) groups according to the duration of drug use: Group A: consists of (12) patients with a

mean age was (51±6) years, they used Captopril for a period of (1-5) years.

Group B: consists of (12) patients with a mean age of (56±6) years, they used Captopril for a period of (6-12) years.

Also, a comparative study was down between Captopril and Atenolol (β-blocker), and their effects on CK-MB levels.

24 patients using Atenolol as antihypertensive drug were included and subdivided into two groups:-

Group A: consists of (12) patients with a mean age (56±6) years, they used Atenolol for a period of (1-5) years.

Group B: consists of (12) patients with a mean age of (60±6) years, they used Atenolol for a period of (6-12) years.

Venous blood samples were obtained from each patient of both groups for measuring the level of CK-MB.

The method used for measuring CK-MB is immunoinhibition assay (RANDOX) in which an antibody is incorporated in the CK reagent. This antibody will bind to and inhibit the activity of the M subunit of CK-MB. This means that only the activity of the B subunit in serum is measured [13, 14].

The sample is serum, heparinized or EDTA plasma. Hemolysis interferes with the assay.

Reagents are mixture of CK-MB buffer/glucose (imidazole buffer, glucose, Mg-acetate and EDTA) with enzymes/coenzymes/substrate/antibody (ADP, AMP, diadenosine pentaphosphate, NADP, HK, G-6-PDH, N-acetylcysteine, creatine phosphate and antibody to CK-M).

Patient's sample is added to the reagent mixture, read the absorbance directly at 340nm (A_1), the second reading is after five minutes exactly (A_2).

$\Delta A = A_2 - A_1$

ΔA multiplied by 1651 (kit factor) gives the concentration of CK-MB in u/L. This procedure is done at room temperature 25°C.

Results:

After collection and categorization of data from the (48) patients included in the study for both Captopril (24) patients and Atenolol (24) patients, statistical analysis was done:

1-For Captopril using patients [table 1] which revealed that, the correlation between Captopril duration (years) and CK-MB (u/L) in total (24) patients included in the study is significant ($p<0.05$) with direct correlation.

2-For Atenolol using patients [table 2] which revealed that, the correlation between Atenolol duration (years) and KB-MB (u/L) in total (24) patients included in the study is significant ($p<0.05$) with direct correlation.

3-The correlation between Captopril, Atenolol for duration of (1-5) years and CK-MB (u/L) in patients included in the study is not significant ($p=0.085$) [table 3].

4-The correlation between Captopril, Atenolol for duration of (6-12) years and CK-MB (u/L) in patients included in the study is significant ($p=0.003$) [table 3].

Table 1: The CK MB (u/L) concentration by duration of use of Captopril in hypertensive patients

Drug type and duration of use (years)	CK MB (u/L)			
	Mean	**SD**	**Minimum**	**Maximum**
Captopril 1-5 years	5.12	2.97	1.60	9.90
6-12 years	10.70	2.06	7.00	13.20
P value	**t=5.350;d.f.=22;P=0.0001***			

Table 2: The CK MB (u/L) concentration by duration of use of Atenolol in hypertensive patients

Drug type and duration of use (years)	CK MB (u/L)			
	Mean	**SD**	**Minimum**	**Maximum**
Atenolol 1-5 years	9.93	8.74	1.60	28.00
6-12 years	20.13	9.64	6.00	36.30
P value	**t=5.350;d.f.=22;P=0.0001***			

*Significant difference at 0.05 level of significance

Table 3: The CK MB (u/L) concentration by duration of use of Captopril and Atenolol in hypertensive patients

Duration of use (years) and drug type	CK MB (u/L)			
	Mean	**SD**	**Minimum**	**Maximum**
1-5 years Captopril	5.12	2.97	1.60	9.90
Atenolol	9.93	8.74	1.60	28.00
P value	**t=1.805;d.f.=22;P=0.085**			
6-12 years Captopril	10.70	2.06	7.00	13.20
Atenolol	20.13	9.64	6.00	36.30
P value	**t=3.316;d.f.=22;P=0.003***			

*Significant difference at 0.05 level of significance

Discussion:

Captopril is one of ACET [15], it has beneficial effects in hypertension and heart failure appears to result primarily from suppression of the renin-angiotensin-aldosterone system [16].

ACE is located on the luminal surface of capillary endothelial cells, particularly in the lungs, and there are also renin-angiotensin systems in many organs like brain and heart [5].

Like many drugs long term use of Captopril may cause different side effects [17], it may be one of cardiovascular diseases like myocardial infarction. To prove the relationship between Captopril and cardiovascular diseases by measurement of creatinine kinase-MB isoenzyme as diagnostic indicator in early and long term use of this drug by hypertensive patients[7]. Rise of the level of this isoenzyme (CK-MB) has been reported in hypertension with myocardial infarction patients [18]. Enzymes always have been identified as specific and sensitive markers of both clinical and subclinical myocardial injury [19]. These enzymes like (CK-MB) are tightly bound to the contractive apparatus and therefore plasma concentrations is extremely low with acute myocardial injury there is a release of CK-MB into the serum, the extent of the elevation in serum depends on the severity of the myocardial injury. And the entry of this enzyme in circulation depends upon the rate of passive diffusion of the enzyme from infarct myocardium cells [2].

An increased levels of CK-MB in serum, is directly proportion to the duration of usage for both Captopril and Atenolol in hypertensive patients. The level of CK-MB of patients who were given Captopril found to have less effect on myocardium than Atenolol. Only about (24) percent of hypertensive patients using Captopril for more than 5 years have an increase levels of CK-MB more than normal level>10 u/L. This is due to alteration in activity of ACE localized on endothelium cells [21], endothelial cells may be the target of ACE inhibitors (one of these Captopril) [22].

Captopril was the first ACE inhibitor developed & was characterized by its novel mechanism which is based on its vasodilatation and inhibition of some renal function activities. These benefits are most clearly seen in hypertension, congestive heart

failure and in diabetic nephropathy. Additionally, it has shown mood elevating properties in some patients.

For hypertensive patients, if long term usage of Captopril, checking should be followed to make sure that if any symptoms of cardiac injury appear. Captopril is preferred to be used for hypertensive patients than Atenolol. Its effect on myocardium is significantly less than Atenolol.

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